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=> stress (w) response and coli and strain and mutant STRESS IS NOT A RECOGNIZED COMMAND
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=> s li and exogenous L2 820 LI AND EXOGENOUS

=> s 12 and lyase

L3 2 L2 AND LYASE

=> 12 and peroxide

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=> s 12 and peroxide

L4 5 L2 AND PEROXIDE

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#### => d ibib abs 13 1-2

ANSWER 1 OF 2 MEDLINE on STN L3 ACCESSION NUMBER: 2004519266 MEDLINE DOCUMENT NUMBER: PubMed ID: 15466221

Unique and overlapping expression patterns among the TITLE: Arabidopsis 1-amino-cyclopropane-1-carboxylate synthase

gene family members.

AUTHOR: Tsuchisaka Atsunari; Theologis Athanasios

CORPORATE SOURCE: Plant Gene Expression Center, Albany, California 94710,

SOURCE: Plant physiology, (2004 Oct) Vol. 136, No. 2, pp.

2982-3000. Electronic Publication: 2004-10-01.

Journal code: 0401224. ISSN: 0032-0889.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

English LANGUAGE:

Priority Journals FILE SEGMENT:

GENBANK-AY680407; GENBANK-AY680408; GENBANK-AY680409; OTHER SOURCE:

> GENBANK-AY680410; GENBANK-AY680411; GENBANK-AY680412; GENBANK-AY680413; GENBANK-AY680414; GENBANK-AY680415; GENBANK-AY680416; GENBANK-AY680417; GENBANK-AY680418; GENBANK-AY680419; GENBANK-AY680420; GENBANK-AY680421; GENBANK-AY680422; GENBANK-AY680423; GENBANK-AY680424

ENTRY MONTH:

ENTRY DATE: Entered STN: 19 Oct 2004

> Last Updated on STN: 4 Jan 2005 Entered Medline: 3 Jan 2005

1-Aminocyclopropane-1-carboxylate synthase (ACS) catalyzes the rate-limiting step in the ethylene biosynthetic pathway in plants. Arabidopsis genome encodes nine ACS polypeptides that form eight functional (ACS2, ACS4-9, and ACS11) homodimers and one nonfunctional (ACS1) homodimer. Transgenic Arabidopsis lines were constructed expressing the beta-glucuronidase (GUS) and green fluorescence protein (GFP) reporter genes from the promoter of each of the gene family members to determine their patterns of expression during plant development. All genes, except ACS9, are expressed in 5-d-old etiolated or light-grown seedlings yielding distinct patterns of GUS staining. ACS9 expression is detected later in development. Unique and overlapping expression patterns were detected for all the family members in various organs of adult plants. ACS11 is uniquely expressed in the trichomes of sepals and ACS1 in the replum. Overlapping expression was observed in hypocotyl, roots, various parts of the flower (sepals, pedicle, style, etc.) and in the stigmatic and abscission zones of the silique. Exogenous indole-3-acetic acid (IAA) enhances the constitutive expression of ACS2, 4, 5, 6, 7, 8, and 11 in the root. Wounding of hypocotyl tissue inhibits the constitutive expression of ACS1 and ACS5 and induces the expression of ACS2, 4, 6, 7, 8, and 11. Inducers of ethylene production such as cold, heat, anaerobiosis, and Li(+) ions enhance or suppress the expression of various members of the gene family in the root of light-grown seedlings. Examination of GUS expression in transverse sections of cotyledons reveals that all ACS genes, except ACS9, are expressed in the epidermis cell layer, guard cells, and vascular tissue. Similar analysis with root tip tissue treated with IAA reveals unique and overlapping expression patterns in the various cell types of the lateral root cap, cell division, and cell expansion zones. IAA inducibility is gene-specific and cell type-dependent across the root tip zone. This limited comparative exploration of ACS gene family expression reveals constitutive spatial and temporal expression patterns of all gene family members throughout the growth period examined. The unique and overlapping

gene activity pattern detected reveals a combinatorial code of spatio-temporal coexpression among the various gene family members during plant development. This raises the prospect that functional ACS heterodimers may be formed in planta.

L3 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:325152' BIOSIS DOCUMENT NUMBER: PREV200600317296

TITLE: Methionine-stress: A pleiotropic approach in enhancing the

efficacy of chemotherapy.

AUTHOR(S): Kokkinakis, Demetrius A. [Reprint Author]

CORPORATE SOURCE: Univ Pittsburgh, Dept Pathol, 5117 Ctr Ave, Pittsburgh, PA

15213 USA

kokkinakisdm@upmc.edu

SOURCE: Cancer Letters, (FEB 28 2006) Vol. 233, No. 2, pp. 195-207.

CODEN: CALEDQ. ISSN: 0304-3835.

DOCUMENT TYPE: Article

General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jun 2006.

Last Updated on STN: 21 Jun 2006

Malignant cells fail to utilize homocysteine (FICYS) in place of methionine (MET) and they are dependent on exogenous MET for In animals, reduction of plasma MET to < 5 mu M can be induced by combined dietary restriction of MET and administration of L-methionine-alpha-deamino-gamma-lyase (methioninase). treatment, terined Lis MET-stress, inhibits the growth of brain tumor xenografts in athymic mice and enhances the efficacy of DNA alkylating chemotherapeutic agents. The response of tumors to MET-stress depends on their mutational status, however, it always involves inhibition of CDK1 and in most cases the upregulation of p21, p27, GADDs and 14-3-3 sigma in response to upregulation of TGF-beta, IRF-1, TNF-alpha, Rb and/or MDA-7 and the downregulation of P13K, RAS and NF-kappa B. Although inhibition of the cell cycle and mitosis is not necessarily dependent oil the tumor's p53 status, the expression of p21, GADD45 and apoptosis related genes (BAX, BCL-2) are regulated by wt-p53, ill addition to their regulation by TGF-beta or MDA-7 in mutated p53 tumors. Mutational variability determines the mode of death (mitotic catastrophe versus apoptosis) in tumor cells subjected to MET-stress. The increase of the efficacy of alkylating agents is related to marked inhibition of O(6-)rnethylquanine-DNA methyltransferase (MGMT) expression, the induction of cell cycle check points and the inhibition of pro-survival pathways by MET-stress. (c) 2005 Elsevier Ireland Ltd. All rights reserved.

#### => d ibib abs 14 1-5

L4 ANSWER 1 OF 5 MEDLINE ON STN ACCESSION NUMBER: 88048324 MEDLINE DOCUMENT NUMBER: PubMed ID: 2823711

TITLE: Effect of lipid hydroperoxide on Xenopus oocytes and on

neurotransmitter receptors synthesized in Xenopus oocytes

injected with exogenous mRNA.

AUTHOR: Aoshima H; Anan M; Ishii H

CORPORATE SOURCE: Department of Chemistry, Faculty of Liberal Arts, Yamaguchi

University, Japan.

SOURCE: Archives of biochemistry and biophysics, (1987 Nov 1) Vol.

258, No. 2, pp. 324-31.

Journal code: 0372430. ISSN: 0003-9861.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198711

ENTRY DATE: Entered STN: 5 Mar 1990

Last Updated on STN: 5 Mar 1990 Entered Medline: 27 Nov 1987

The effect of 13-L-hydroperoxylinoleic acid (LOOH) on both Xenopus oocytes AB and neurotransmitter receptors synthesized in the oocytes was studied by electrophysiological and ion flux measurement. Addition of LOOH to the incubation mixture of the oocytes raised the membrane potential and decreased the membrane resistance of the oocytes. These effects of LOOH on the oocytes were reversed within a few hours by incubation with frog Ringer solution. Addition of LOOH also caused an increase of Li + and 45Ca2+ uptake into the oocytes. However, production of alkoxy radicals by the addition of FeCl2 to the incubation mixture containing LOOH did not accelerate the damage to the oocytes by LOOH. So essential toxicity is caused possibly by an increase in the membrane permeability resulting from disturbance of the lipid bilayer arrangement, not from production of active alkoxy radicals during decomposition of LOOH. Nicotinic acetylcholine and gamma-aminobutyric acid receptors were synthesized in Xenopus oocytes by injecting mRNA prepared from Electrophorus electricus electroplax and rat brain. LOOH noncompetitively inhibited the function of these receptors and also increased the rate of desensitization of the receptors.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:910375 CAPLUS

DOCUMENT NUMBER: 138:166684

TITLE: Role of hydrogen peroxide in salicylic

acid-induced stomatal closure in Vicia faba guard

cells

AUTHOR(S): Dong, Facai; Wang, Pengtao; Zhang, Lin; Song, Chunpeng

CORPORATE SOURCE: Department of Biology, Henan University, Kaifeng,

475001, Peop. Rep. China

SOURCE: Zhiwu Shengli Xuebao (2001), 27(4), 296-302

CODEN: CWSPDA; ISSN: 0257-4829

PUBLISHER: Kexue Chubanshe

DOCUMENT TYPE: Journal LANGUAGE: English.

Many plant pathogens can penetrate leaf tissues through stomatal opening, so narrowing stomatal apertures may be advantageous for plant defense. The evidence was provided that H2O2 may function as an intermediate in salicylic acid (SA) signal in guard cells by epidermal strips bioassay and laser scanning confocal microscopy. SA can induce stomatal closure with a concentration-dependent manner, and H2O2 has the similar effect as SA. The effect of stomatal closure induced by SA at 100 µmol/L could be reversed evidently by CAT 20 U/mL or Vc 10 mmol/L, resp., but CAT or Vc alone treatment promoted stomatal opening slightly over the control. course expts. of single-cell assay based on fluorescent probe DCFH showed that the generation of H2O2 in guard cells could be induced by exogenous (Plate I) or endogenous SA 100 µmol/L (Plate LI) by directly addition or microinjection into one guard cell of a stoma, but distilled water microinjection as control caused no changes in DCFH fluorescent (Plate LI). These results suggest that the plant infected by pathogens may close their stomata via a pathway involving H2O2 production, thus interfering with the continuous invasion of pathogens through the stomatal pores.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:612284 CAPLUS

DOCUMENT NUMBER: 107:212284

TITLE: Effect of lipid hydroperoxide on Xenopus oocytes and

on neurotransmitter receptors synthesized by Xenopus

oocytes injected with exogenous mRNA

AUTHOR(S): Aoshima, Hitoshi; Anan, Makoto; Ishii, Hisashi

CORPORATE SOURCE: Fac. Liberal Arts, Yamaguchi Univ., Yamaguchi, 753,

Japan

SOURCE: Archives of Biochemistry and Biophysics (1987),

258(2), 324-31

CODEN: ABBIA4; ISSN: 0003-9861

DOCUMENT TYPE: Journal LANGUAGE: English

AB The effect of 13-L-hydroperoxylinoleic acid (LOOH) on both Xenopus oocytes and neurotransmitter receptors synthesized in the oocytes was studied by electrophysiol. and ion flux measurement. Addition of LOOH to the incubation mixture of the oocytes raised the membrane potential and decreased the membrane resistance of the oocytes. These effects of LOOH on the oocytes were reversed within a few hours by incubation with frog Ringer solution Addition of LOOH also caused an increase of Li+ and 45Ca2+ uptake into the oocytes. However, production of alkoxy radicals by the addition of FeCl2 to the incubation mixture containing LOOH did not accelerate the damage

the oocytes by LOOH. So essential toxicity is caused possibly by an increase in the membrane permeability resulting from disturbance of the lipid bilayer arrangement, not from production of active alkoxy radicals during decomposition of LOOH. Nicotinic acetylcholine and GABA receptors were synthesized in Xenopus oocytes by injecting mRNA prepared from Electrophorus electricus electroplax and rat brain. LOOH non-competitively inhibited the function of these receptors and also increased the rate of desensitization of the receptors.

L4 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1995:25250710 BIOTECHNO

TITLE: The oxidation of hemocyanin. Kinetics, reaction

mechanism and characterization of Met-hemocyanin

product

AUTHOR: Beltramini M.; Bubacco L.; Casella L.; Alzuet G.;

Gullotti M.; Salvato B.

CORPORATE SOURCE: Department of Biology, Via Trieste 75, I-35131 Padova,

Italy.

SOURCE: European Journal of Biochemistry, (1995), 232/1

(98-105)

CODEN: EJBCAI ISSN: 0014-2956

DOCUMENT TYPE:

AB

to

Journal; Article

DOCUMENT TIPE: SOUTHAI, ALCICLE

COUNTRY: Germany, Federal Republic of

LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25250710 BIOTECHNO

The reaction that gives met-hemocyanin from Octopus vulgaris oxy-hemocyanin has been reinvestigated under several experimental conditions. Various anions including azide, fluoride and acetate have been found to promote this reaction. Kinetic data indicate that the reaction mechanism is different from that currently accepted involving a peroxide displacement of bound dioxygen through an associative chemistry on an open axial position of the copper ions ¢Hepp, A. F., Himmelwright, R. S., Eickman, N. C. and Solomon, E. I. (1979) Biochem. Biophys. Res. Commun. 89, 1050-1057; Solomon, E. I. in Copper proteins (Spiro, T. G., ed.) pp. 43-108, J. Wiley, New York!. Our study suggests that the protonated form of the anion is Likely to be the species reacting with the oxygenated form of the protein. Furthermore, it is also proposed that protonation of bound dioxygen generates an intermediate hydroperoxo-dicopper(II) complex to which the exogenous anion is also bound. This intermediate in not accumulated and precedes the release of hydrogen peroxide by reaction with water. Upon dialysis it leads to the met-hemocyanin form. The structure of this dinuclear copper(II) derivative contains a di- $\mu$ -hydroxo bridge but there is evidence from optical and circular dichroism spectra for partial protonation of these bridges at low pH. As a consequence, while one azide molecule binds in the bridging mode to

met-hemocyanin with low affinity (K = 30 M.sup.-.sup.1) at pH 7.0, it binds with much higher affinity at pH 5.5 (K = 1500 M.sup.-.sup.1), where a second azide ligand also binds in the terminal mode (K = 20 M.sup.-.sup.1). The coordination mode of the azide ligands is deduced from the optical and circular dichroism spectra of the protein complexes.

L4 ANSWER 5 OF 5 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights

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ACCESSION NUMBER: 95250500 EMBASE

DOCUMENT NUMBER: 1995250500

TITLE: The oxidation of hemocyanin. Kinetics, reaction mechanism

and characterization of Met-hemocyanin product.

AUTHOR: Beltramini M.; Bubacco L.; Casella L.; Alzuet G.; Gullotti

M.; Salvato B.

CORPORATE SOURCE: Department of Biology, Via Trieste 75, I-35131 Padova, Italy

SOURCE: European Journal of Biochemistry, (1995) Vol. 232, No. 1,

pp. 98-105. .

ISSN: 0014-2956 CODEN: EJBCAI

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 12 Sep 1995

Last Updated on STN: 12 Sep 1995

AB The reaction that gives met-hemocyanin from Octopus vulgaris oxy-hemocyanin has been reinvestigated under several experimental conditions. Various anions including azide, fluoride and acetate have been found to promote this reaction. Kinetic data indicate that the reaction mechanism is different from that currently accepted involving a peroxide displacement of bound dioxygen through an associative chemistry on an open axial position of the copper ions [Hepp, A. F., Himmelwright, R. S., Eickman, N. C. and Solomon, E. I. (1979) Biochem. Biophys. Res. Commun. 89, 1050-1057; Solomon, E. I. in Copper proteins (Spiro, T. G., ed.) pp. 43-108, J. Wiley, New York]. Our study suggests that the protonated form of the anion is Likely to be the species reacting with the oxygenated form of the protein. Furthermore, it is also proposed that protonation of bound dioxygen generates an intermediate hydroperoxo-dicopper(II) complex to which the exogenous anion is also bound. This intermediate in not accumulated and precedes the release of hydrogen peroxide by reaction with water. Upon dialysis it leads to the met-hemocyanin form. The structure of this dinuclear copper( 11) derivative contains a  $di-\mu$ -hydroxo bridge but there is evidence from optical and circular dichroism spectra for partial protonation of these bridges at low pH. As a consequence, while one azide molecule binds in the bridging mode to met-hemocyanin with low affinity (K = 30 M-1) at pH 7.0, it binds with much higher affinity at pH 5.5 (K =1500 M-1), where a second azide ligand also binds in the terminal mode (K = 20 M-1). The coordination mode of the azide ligands is deduced from the optical and circular dichroism spectra of the protein complexes.

Application/Control Number: 10/750,955 Page 7

Art Unit: 2834

applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

- (I) <u>Sequence Listing.</u> See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.
- 6. A substitute specification, drawings and claims are required pursuant to 37 CFR 1.125(a) because provided disclosure and claims are not in proper format as required by the MPEP.

A substitute specification must not contain new matter. The substitute specification must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. An accompanying clean version (without markings) and a statement that the substitute specification contains no new matter must also be supplied. Numbering the paragraphs of the specification of record is not considered a change that must be shown.

Application/Control Number: 10/750,955 Page 8

Art Unit: 2834

# Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite

for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention.

The claim 1 is is generally narrative and indefinite, failing to conform with current U.S. practice, because the language of the claim 1 does not provide desired clarity and precision, since the scope of the invention sought to be patented cannot be determined from the language of the claim with a reasonable degree of certainty. *In re Wiggins*,

488 F.2d 538, 179 USPQ 421 (CCPA 1973).

## Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. As far as it can be understood and interpreted. Claim 1 is rejected under 35

U.S.C. 102(b) as being clearly anticipated by Carlson (US 3,894,393).

As broadly as it can be interpreted, no feature in the claim distinguish itself from the prior art.

# Page 9

#### Conclusion

- 11. The prior art made of record and not relied upon is considered pertinent to applicant(s) disclosure.
- 12. When the claims are amended, applicant(s) should state in detail where in the original disclosure or in the drawings the amended features find support. **No new matter may be introduced**.
- 13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicholas Ponomarenko whose telephone number is (571) 272- 2033, Fax: (571) 273-2033, or to his SPE Darren Schuberg (571) 272-2044.
- 14. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 2800 Customer Service Phone: (571) 272-2815

np June 16, 2005

> Nicholas Ponomarenko Primary Examiner Technology Center 2800